

# INTERNATIONAL SEARCH REPORT

PCT/GB2004/004274

**A. CLASSIFICATION OF SUBJECT MATTER**  
 IPC 7 A61K35/74 A61K39/095

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
 IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, EMBASE

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	PEETERS C C A M ET AL: "Phase I clinical trial with a hexavalent PorA containing meningococcal outer membrane vesicle vaccine" VACCINE, BUTTERWORTH SCIENTIFIC. GUILDFORD, GB, vol. 14, no. 10, July 1996 (1996-07), pages 1009-1015, XP004057633 ISSN: 0264-410X page 1010, left-hand column, paragraph 1 - paragraph 2 page 1014, right-hand column, paragraph 1 ----- -/-	1-17, 31, 32, 36
Y	-----	26

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

\* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the International filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the International filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

11 August 2005

Date of mailing of the international search report

09.09.2005

Name and mailing address of the ISA

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>BOULTON IAN C ET AL: "Neisserial binding to CEACAM1 arrests the activation and proliferation of CD4+ T lymphocytes." NATURE IMMUNOLOGY. MAR 2002, vol. 3, no. 3, March 2002 (2002-03), pages 229-236, XP002323222 ISSN: 1529-2908 the whole document</p> <p>-----</p>	1-12, 23-25, 31-36
Y		26
P, X	<p>WO 2004/014417 A (GLAXOSMITHKLINE BIOLOGICALS SA; BIEMANS, RALPH; DENOEL, PHILIPPE; FERO) 19 February 2004 (2004-02-19) page 4 - page 5; claims 6,9,11,17,19</p> <p>-----</p>	1-4, 9-17,31, 32,36
A	<p>COHEN M S ET AL: "Human experimentation with Neisseria gonorrhoeae: progress and goals." THE JOURNAL OF INFECTIOUS DISEASES. MAR 1999, vol. 179 Suppl 2, March 1999 (1999-03), pages S375-S379, XP002323375 ISSN: 0022-1899 the whole document</p> <p>-----</p>	23,24, 26,33-35
A	<p>VAN DER LEY P ET AL: "Construction of Neisseria meningitidis strains carrying multiple chromosomal copies of the porA gene for use in the production of a multivalent outer membrane vesicle vaccine" VACCINE, BUTTERWORTH SCIENTIFIC. GUILDFORD, GB, vol. 13, no. 4, 1995, pages 401-407, XP004057740 ISSN: 0264-410X the whole document</p> <p>-----</p>	1-4, 9-15,17, 31-36
A	<p>LEY VAN DER P ET AL: "CONSTRUCTION OF A MULTIVALENT MENINGOCOCCAL VACCINE STRAIN BASED ONTHE CLASS 1 OUTER MEMBRANE PROTEIN" INFECTION AND IMMUNITY, AMERICAN SOCIETY FOR MICROBIOLOGY. WASHINGTON, US, vol. 60, no. 8, August 1992 (1992-08), pages 3156-3161, XP000946454 ISSN: 0019-9567 the whole document</p> <p>-----</p>	1-17,23, 24,26, 31-36

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>WIERTZ E J ET AL: "T-cell responses to outer membrane proteins of <i>Neisseria meningitidis</i>: comparative study of the Opa, Opc, and PorA proteins"  <i>INFECTION AND IMMUNITY, AMERICAN SOCIETY FOR MICROBIOLOGY</i>. WASHINGTON, US, vol. 64, no. 1, January 1996 (1996-01), pages 298-304, XP002127427  ISSN: 0019-9567  the whole document</p> <p>-----</p>	1-17,23, 24,26, 31-36
A	<p>WEDEGE ELISABETH ET AL: "Antibody specificities and effect of meningococcal carriage in icelandic teenagers receiving the Norwegian serogroup B outer membrane vesicle vaccine."  <i>INFECTION AND IMMUNITY</i>. JUL 2003, vol. 71, no. 7, July 2003 (2003-07), pages 3775-3781, XP002322410  ISSN: 0019-9567  the whole document</p> <p>-----</p>	1-17,23, 24,26, 31-36
A	<p>CLAASSEN I ET AL: "Production, characterization and control of a <i>Neisseria meningitidis</i> hexavalent class 1 outer membrane protein containing vesicle vaccine"  <i>VACCINE, BUTTERWORTH SCIENTIFIC</i>. GUILDFORD, GB, vol. 14, no. 10, July 1996 (1996-07), pages 1001-1008, XP004057632  ISSN: 0264-410X  the whole document</p> <p>-----</p>	1-17,23, 24,26, 31-36
A	<p>WO 03/051379 A (HEALTH PROTECTION AGENCY; FOSTER, KEITH, ALAN; GORRINGE, ANDREW, RICHA) 26 June 2003 (2003-06-26)  the whole document</p> <p>-----</p>	1-17,23, 24,26, 31-36
A	<p>NORMARK STAFFAN ET AL: "Gonococci cause immunosuppression by engaging a coinhibitory receptor on T lymphocytes."  <i>NATURE IMMUNOLOGY</i>. MAR 2002, vol. 3, no. 3, March 2002 (2002-03), pages 210-211, XP002323223  ISSN: 1529-2908  the whole document</p> <p>-----</p>	1-17,23, 24,26, 31-36

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# INTERNATIONAL SEARCH REPORT

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>GRAY-OWEN S D ET AL: "CD66 carcinoembryonic antigens mediate interactions between Opa-expressing Neisseria gonorrhoeae and human polymorphonuclear phagocytes." THE EMBO JOURNAL. JUN 1997, vol. 16, no. 12, June 1997 (1997-06), pages 3435-3445, XP002323383 ISSN: 0261-4189 the whole document</p> <p>-----</p> <p>KUPSCHE E M ET AL: "Variable opacity (Opa) outer membrane proteins account for the cell tropisms displayed by Neisseria gonorrhoeae for human leukocytes and epithelial cells." THE EMBO JOURNAL. FEB 1993, vol. 12, no. 2, February 1993 (1993-02), pages 641-650, XP008045296 ISSN: 0261-4189 the whole document</p> <p>-----</p> <p>DEHIO C ET AL: "The role of neisserial Opa proteins in interactions with host cells." TRENDS IN MICROBIOLOGY. DEC 1998, vol. 6, no. 12, December 1998 (1998-12), pages 489-495, XP002340390 ISSN: 0966-842X table 1</p> <p>-----</p>	1-17, 23, 24, 26, 31-36
X	<p>GRANT C C ET AL: "Proteoglycan receptor binding by Neisseria gonorrhoeae MS11 is determined by the HV-1 region of OpaA." MOLECULAR MICROBIOLOGY. APR 1999, vol. 32, no. 2, April 1999 (1999-04), pages 233-242, XP002340391 ISSN: 0950-382X page 239 - page 240; figures 2, 4</p> <p>-----</p> <p>VAN PUTTEN J P ET AL: "Binding of syndecan-like cell surface proteoglycan receptors is required for Neisseria gonorrhoeae entry into human mucosal cells." THE EMBO JOURNAL. 15 MAY 1995, vol. 14, no. 10, 15 May 1995 (1995-05-15), pages 2144-2154, XP002340392 ISSN: 0261-4189 page 2151, right-hand column, paragraph 4; figure 8 page 2153, right-hand column, paragraph 1</p> <p>-----</p>	37, 38
X		18-21, 27-30, 39-43
	-/-	

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>GRAY-OWEN S D ET AL: "Differential Opa specificities for CD66 receptors influence tissue interactions and cellular response to <i>Neisseria gonorrhoeae</i>." <i>MOLECULAR MICROBIOLOGY</i>. DEC 1997, vol. 26, no. 5, December 1997 (1997-12), pages 971-980, XP002340393 ISSN: 0950-382X table 1</p> <p>-----</p> <p>BOS M P ET AL: "Carcinoembryonic antigen family receptor recognition by gonococcal Opa proteins requires distinct combinations of hypervariable Opa protein domains" <i>INFECTION AND IMMUNITY, AMERICAN SOCIETY FOR MICROBIOLOGY</i>. WASHINGTON, US, vol. 70, no. 4, April 2002 (2002-04), pages 1715-1723, XP002322409 ISSN: 0019-9567 page 1716, right-hand column, last paragraph</p> <p>-----</p> <p>BILLKER O ET AL: "The structural basis of CEACAM-receptor targeting by neisserial Opa proteins." <i>TRENDS IN MICROBIOLOGY</i>. JUN 2000, vol. 8, no. 6, June 2000 (2000-06), pages 258-260 ; dis, XP002340394 ISSN: 0966-842X the whole document</p> <p>-----</p> <p>BOS M P ET AL: "Differential recognition of members of the carcinoembryonic antigen family by Opa variants of <i>Neisseria gonorrhoeae</i>." <i>INFECTION AND IMMUNITY</i>. JUN 1997, vol. 65, no. 6, June 1997 (1997-06), pages 2353-2361, XP002340395 ISSN: 0019-9567 the whole document</p> <p>-----</p> <p>DE JONGE MARIEN I ET AL: "Conformational analysis of opacity proteins from <i>Neisseria meningitidis</i>." <i>EUROPEAN JOURNAL OF BIOCHEMISTRY / FEBS</i>. NOV 2002, vol. 269, no. 21, November 2002 (2002-11), pages 5215-5223, XP002340396 ISSN: 0014-2956 page 5220, right-hand column, paragraph 2</p> <p>-----</p>	1-21, 23-43
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**C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT**

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	VIRJI M ET AL: "The N-domain of the human CD66a adhesion molecule is a target for Opa proteins of <i>Neisseria meningitidis</i> and <i>Neisseria gonorrhoeae</i> ." MOLECULAR MICROBIOLOGY. DEC 1996, vol. 22, no. 5, December 1996 (1996-12), pages 929-939, XP002340397 ISSN: 0950-382X page 934, right-hand column, paragraph 1 -----	1-21, 23-43
A	US 2003/059444 A1 (ZOLLINGER WENDELL D ET AL) 27 March 2003 (2003-03-27) page 5, paragraph 60 -----	1-21, 23-43

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## Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:  
Although claims 23–26, 31, 33–35 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2.  Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:  
**1–21, 23–43 (all where relating to inventions 1 and 2 only)**
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- The additional search fees were accompanied by the applicant's protest.  
 No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-12, 23, 24, 26, 31-36 (all partially), 13-17 (all completely)

a method of selecting or preparing microorganisms,  
compositions or vaccines that are free of OPA for treatment  
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2. claims: 1-12, 23, 24, 26, 31-36 (all partially),  
18-21, 25, 27-30, 37-43 (all completely)

a method of selecting or preparing microorganisms,  
compositions or vaccines that contain OPA which does not  
bind to CEACAM1 for treatment  
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3. claims: 22 (completely), 36 (partially)

a composition comprising Neisseria outer membrane vesicles  
which comprise an antagonist which inhibits binding of Opa  
to CEACAM1  
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# INTERNATIONAL SEARCH REPORT

Information on patent family members

PCT/GB2004/004274

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 2004014417	A	19-02-2004	AU 2003250204 A1 AU 2003253375 A1 AU 2003260357 A1 AU 2003269864 A1 BR 0313100 A CA 2489030 A1 CA 2493092 A1 CA 2493124 A1 CA 2493977 A1 WO 2004014419 A1 WO 2004014417 A2 WO 2004015099 A2 WO 2004014418 A2 EP 1524990 A2 EP 1524991 A1 EP 1524992 A2 EP 1524993 A2 AU 2003273854 A1 CA 2496045 A1 WO 2004020452 A2 EP 1532168 A2 AU 2003287945 A1 CA 2495086 A1 WO 2004020463 A2	25-02-2004 25-02-2004 25-02-2004 25-02-2004 21-06-2005 19-02-2004 19-02-2004 19-02-2004 19-02-2004 19-02-2004 19-02-2004 19-02-2004 19-02-2004 19-02-2004 19-02-2004 19-02-2004 19-02-2004 19-02-2004 27-04-2005 27-04-2005 27-04-2005 27-04-2005 19-03-2004 11-03-2004 11-03-2004 25-05-2005 19-03-2004 11-03-2004 11-03-2004
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